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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/808,275	03/14/2001	Randall W. Nelson	41821.0237	4255

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EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/808,275	NELSON ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-47* is/are pending in the application.

4a) Of the above claim(s) *31-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The amendment and declaration filed April 28, 2004 is acknowledged and has been entered.

Double Patenting

Claims 31, 36 and 41 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of copending Application No. 09/808314. Although the conflicting claims are not identical, they are not patentably distinct from each other because it would have been obvious to one of ordinary skill in the art to determine and identify the analyte by using mass spectrometery for molecular weight analysis.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 41 is vague and indefinite because it is unclear what relationship exits between the different antibodies and the analyte. For example, in the case in which only one analyte species is detected. Does the different antibodies bind to different

epitopes of the analyte or is one antibody bound to the other antibody which in turn binds to the analyte. Please clarify.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

2. Claims 31, 32, 36, 37, 45 and 46 are rejected under 35 U.S.C. 102(a) as being anticipated by Papac et al (Epitope mapping of the gastrin-releasing peptide/anti-bombesin monoclonal antibody complex by proteolysis followed by matrix-assisted laser desorption ionization mass spectrometry, Protein Science (1994), 3:1485-1492).

Papac et al disclose antibodies immobilized to agarose beads (solid substrate). Papac et al disclose incubating these beads with antigens for a time period to allow the immobilized antibody to bind to the antigen to form a complex (post-combination affinity

reagent) (p. 1486, col 2, Results Section). Papac et al disclose centrifuging the complex and removing supernatant (isolating the post-combination affinity reagent). Papac et al disclose adding matrix (laser desorption/ionization agent) to the antibody/antigen complex (p. 1486, col 2). Papac et al disclose determining the identity of the analyte using mass spectrometry (p. 1486, col 2 and Figure 1). Papac et al disclose determining the analyte by m/z (mass to charge ratio) (Figure 1).

3. Claims 31 and 36 are rejected under 35 U.S.C. 102(e) as being anticipated by Hutchens et al (US 5,894,063).

Hutchens et al disclose a method for the detection of analytes (col 3, lines 50-59). Hutchens et al disclose that the analyte of interest can be captured by immobilized antibodies. Hutchens et al disclose that the antibodies are immobilized to solid surfaces (solid substrates) (col 6, line 64 – col 7, line 13). Hutchens et al disclose that the captured analytes can be washed to remove any contaminants and transferred to the probe surface (col 5, lines 10-20). Hutchens et al disclose that the analytes can be detected and determined by mass analysis (col 5, lines 10-20 and col 1, lines 24-39).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 33 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al (Protein Science) in view of Rampal et al (US 5,437,979).

See above for teachings of Papac et al (Protein Science).

Papac et al (Protein Science) differs from the instant invention in failing to teach combining the affinity reagent with the specimen using a micropipette tip in which there is a filter element which retains the affinity reagent.

Rampal et al disclose a micropipette tip in which solid substrates are retained by porous frits (filter element). Rampal et al disclose that these solid substrates comprise

immobilized reactants, which bind to an analyte of interest. Rampal et al disclose that the use of the micropipette tips in this manner minimizes exposure of the solid phase to the surroundings by retaining the solid phase in an almost fully enclosed environment, thereby enhancing reliability, reproducibility and safety (col 1, lines 35-50).

It would have been obvious to one of ordinary skill in the art to incorporate the beads of Papac et all into a micropipette such as taught by Rampal et al because Rampal et al discloses that these pipette tips can be used in reaction assays and also minimizes exposure of the solid phase to the surroundings by retaining the solid phase in an almost fully enclosed environment, thereby enhancing reliability, reproducibility and safety.

8. Claims 34 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al (Protein Science (1994), 3:1485-1492)) in view of Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS, Analytical Chemistry 194, 66, 2609-2613).

See above for teachings of Papac et al (Protein Science).

Papac et al (Protein Science) differ from the instant invention in failing to disclose adding a disassociation agent to the isolated post-combination affinity reagent prior to the step of adding the laser desorption/ioniztion agent.

Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS) disclose sample preparation can influence the spectra observed and that for immobilized affinity chromatography, a 3 times stronger signal is observed when the supernatant is used for analysis (a dissociation reagent is used before application of the

desorption/ionization agent) compared with mixing the MALDI matrix with the beads on the target (p. 2613, 3rd paragraph) and that immobilized affinity chromatography differs from conventional chromatography in that it exploits specific biological interactions such as those of an antibody and antigen which demonstrate high specificity associated affinity binding and that, either half of a biological interaction can be used in the stationary phase as an immobilized ligand (p. 2609, paragraph 1).

It would have been obvious to one of ordinary skill in the art to incorporate the use of a dissociation reagent as taught by Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS) into the method of Papac et al (Protein Science) because Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS) show that this dissociation reagent allows for a 3 times stronger signal.

9. Claims 35 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al (Protein Science) in view of Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS) as applied to claims 31, 32, 34, 36, 37, 39, 45 and 46 above, and further in view of Rampal et al (US 5,437,979).

See above for the teachings of Papac et al (Protein Science) and Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS).

Papac et al and Papac et al differ from the instant invention in failing to teach combining the affinity reagent with the specimen using a micropipette tip in which there is a filter element which retains the affinity reagent.

Rampal et al disclose a micropipette tip in which solid substrates are retained by porous frits (filter element). Rampal et al disclose that these solid substrates comprise

immobilized reactants, which bind to an analyte of interest. Rampal et al disclose that the use of the micropipette tips in this manner minimizes exposure of the solid phase to the surroundings by retaining the solid phase in an almost fully enclosed environment, thereby enhancing reliability, reproducibility and safety (col 1, lines 35-50). Further, Rampal et al disclose that that bound species may be removed from the solid substrates by conventional means known in the art (col 3).

It would have been obvious to one of ordinary skill in the art to incorporate the beads of Papac et al (Protein Science) into a micropipette such as taught by Rampal et al because Rampal et al discloses that these pipette tips can be used in reaction assays and also minimizes exposure of the solid phase to the surroundings by retaining the solid phase in an almost fully enclosed environment, thereby enhancing reliability, reproducibility and safety.

10. Claim 41 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al (Protein Science) in view of Bangs et al. (Microspheres, part 2: Ligand attachment and test fomulation, IVD Technology Magazine, March 1995).

See above for teachings of Papac et al.

Papac et al differ from the instant invention in failing to teach different antibodies on a solid substrate to produce the affinity reagent.

Bangs et al disclose the adsorption of polyclonal antibodies to microspheres which bind to monoclonal antibodies to form an affinity reagent for an analyte of interest. Bangs et al teaches that the use of these two different antibodies on the microsphere

provides better activity, or recognition of antigen because the second antibody is away from the surface of the microsphere.

It would have been obvious to one of ordinary skill in the art to incorporate different antibodies such as taught by Bangs et al on the beads of Papac et al because Bangs et al shows that the use of two different antibodies on the microsphere provides better activity or recognition of antigen because the second antibody is away from the surface of the microsphere.

11. Claim 42 is rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al (Protein Science) in view of Bangs et al as applied to claims 31, 32, 36, 37, 41, 45 and 46 above, and further in view of Rampal et al (US 5,437,979).

See above for teachings of Papac et al (Protein Science) and Bangs et al.

Papac et al (Protein Science) and Bangs et al differ from the instant invention in failing to teach combining the affinity reagent with the specimen using a micropipette tip in which there is a filter element which retains the affinity reagent.

Rampal et al disclose a micropipette tip in which solid substrates are retained by porous frits (filter element). Rampal et al disclose that these solid substrates comprise immobilized reactants, which bind to an analyte of interest. Rampal et al disclose that the use of the micropipette tips in this manner minimizes exposure of the solid phase to the surroundings by retaining the solid phase in an almost fully enclosed environment, thereby enhancing reliability, reproducibility and safety (col 1, lines 35-50).

It would have been obvious to one of ordinary skill in the art to incorporate the modified beads of Papac et al into a micropipette such as taught by Rampal et al

because Rampal et al discloses that these pipette tips can be used in reaction assays and also minimizes exposure of the solid phase to the surroundings by retaining the solid phase in an almost fully enclosed environment, thereby enhancing reliability, reproducibility and safety.

12. Claim 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al (Protein Science (1994), 3:1485-1492)) in view Bangs et al as applied to claims 31, 32, 36, 37, 41, 45, and 46 above and further in view of Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS, Analytical Chemistry 194, 66, 2609-2613).

See above for teachings of Papac et al (Protein Science) and Bangs et al.

Papac et al (Protein Science) and Bangs et al differ from the instant invention in failing to disclose adding a disassociation agent to the isolated post-combination affinity reagent prior to the step of adding the laser desorption/ioniztion agent.

Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS) disclose sample preparation can influence the spectra observed and that for immobilized affinity chromatography, a 3 times stronger signal is observed when the supernatant is used for analysis (a dissociation reagent is used before application of the desorption/ionization agent) compared with mixing the MALDI matrix with the beads on the target (p. 2613, 3rd paragraph) and that immobilized affinity chromatography differs from conventional chromatography in that it exploits specific biological interactions such as those of an antibody and antigen which demonstrate high specificity associated affinity binding and that, either half of a biological interaction can be used in the stationary phase as an immobilized ligand (p. 2609, paragraph 1).

It would have been obvious to one of ordinary skill in the art to incorporate the use of a dissociation reagent as taught by Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS) into the modified method of Papac et al (Protein Science) because Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS) show that this dissociation reagent allows for a 3 times stronger signal.

13. Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al (Protein Science (1994), 3:1485-1492)) in view Bangs et al and Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS, Analytical Chemistry 194, 66, 2609-2613) as applied to claims 31, 32, 36, 37, 41, 43, 45 and 46 above and further in view of Rampal et al (US 5,437,979).

See above for the teachings of Papac et al (Protein Science) Bangs et al and Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS).

Papac et al., Bangs et al and Papac et al differ from the instant invention in failing to teach combining the affinity reagent with the specimen using a micropipette tip in which there is a filter element which retains the affinity reagent.

Rampal et al disclose a micropipette tip in which solid substrates are retained by porous frits (filter element). Rampal et al disclose that these solid substrates comprise immobilized reactants, which bind to an analyte of interest. Rampal et al disclose that the use of the micropipette tips in this manner minimizes exposure of the solid phase to the surroundings by retaining the solid phase in an almost fully enclosed environment, thereby enhancing reliability, reproducibility and safety (col 1, lines 35-50). Further,

Rampal et al disclose that that bound species may be removed from the solid substrates by conventional means known in the art (col 3).

It would have been obvious to one of ordinary skill in the art to incorporate the modified beads of Papac et al (Protein Science) into a micropipette such as taught by Rampal et al because Rampal et al discloses that these pipette tips can be used in reaction assays and also minimizes exposure of the solid phase to the surroundings by retaining the solid phase in an almost fully enclosed environment, thereby enhancing reliability, reproducibility and safety.

Response to Arguments

The Declaration by Allan L. Bieber filed April 28, 2004 is found persuasive. Therefore, the 102 rejection using the article "Mass Spectrometric Immunoassay" published in Analytical Chemistry 1995, 67, 1153-1158 has been withdrawn. However, a new ground (s) of rejection is made (see above).

Conclusion

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Tarantino et al (US 5,643,800) disclose antibodies bound to porous support. Taraantino et al disclose that these antibodies can be used to search for specific proteins within a complex mixture (col 5, lines 60-67). Tarantino et al disclose that detection can be performed by matrix assisted laser desorption ionization (col 1).

Benninghoven et al (US 4,527,059) a laser activated mass spectrometer having a sample holder for holding a given component to be investigated (abstract).

Benninghoven et al disclose a solid support with a reagent for capturing a substance. Benninghoven disclose that this process can be carried out by antibody/antigen reactions.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary W. Counts
Examiner
Art Unit 1641
June 2, 2004

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